PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of:

Danter, et al.

Serial No.: 10/531,107

Filed: April 11, 2005

For: Protein Tyrosine Kinase Inhibitors

Confirmation No.: 2708

Group Art Unit: 1624

Examiner: RAO, DEEPAK R.

Docket No.: 221904-1030

SECOND PRELIMINARY AMENDMENT

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

In regard to the above-referenced application, the Applicants submit the following preliminary amendments and remarks to be respectively entered and considered prior to examination.

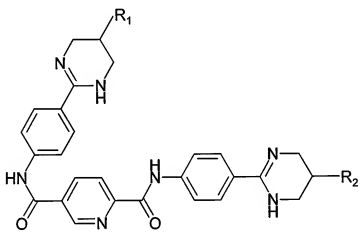
It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 C.F.R. § 1.136(a), and any fees required therefor (including fees for net addition of claims) are hereby authorized to be charged to Deposit Account No. 20-0778.

CURRENT STATUS OF THE CLAIMS

In the Claims

The following is a marked-up version of the claims with the language that is underlined ("___") being added and the language that contains strikethrough ("—") being deleted:

1. (Original) A composition comprising a compound selected from the group consisting of Formula I, a pharmaceutically acceptable salt thereof, a stereoisomer thereof, and mixtures thereof:



Formula I

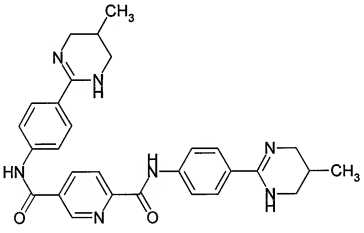
wherein R_1 and R_2 are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; halogen; aryl; heteroaryl containing N, O, or S; the aryl and heteroaryl may be further substituted with halogen, an alkyl, alkenyl, and alkynyl; NZ_1Z_2, wherein Z_1 and Z_2 are independently selected from the group consisting of H and alkyl; and (CO)Y wherein Y is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl containing N, O, or S; with the proviso that when R_1 is hydrogen, R_2 is a group other than hydrogen; and

a pharmaceutically acceptable carrier, wherein the composition is for treatment of cancer involving inappropriate tyrosine kinase activity.

2. (Original) The composition of claim 1, with the proviso that when R_1 is methyl, R_2 is a group other than methyl.

3. (Currently Amended) The ~~compound~~ composition of claim 1, wherein the aryl and heteroaryl are substituted with at least one of a halogen, an alkyl, an alkenyl, and an alkynyl.

4. (Original) The composition of claim 1, wherein the compound is selected from the group consisting of Formula II, a pharmaceutically acceptable salt thereof, a stereoisomer thereof and mixtures thereof:



Formula II

5. (Original) The composition of claim 1, wherein the pharmaceutically acceptable salt is derived from an inorganic acid or an organic acid, wherein the inorganic acid is selected from the group consisting of hydrochloric, hydrobromic, sulfuric, sulfamic, phosphoric, and nitric acids; and the organic acid is selected from the group consisting of acetic, propionic, succinic, glycolic, stearic, lactic, malic, tartaric, citric, ascorbic, pamoic, maleic, hydroxymaleic, phenylacetic, glutamic, benzoic, salicylic, sulfanilic, 2-acetoxy-benzoic, fumaric, toluenesulfonic, methanesulfonic, ethane disulfonic, oxalic, isethionic, and trifluoroacetic acids.

6. (Original) The composition of claim 5, wherein the pharmaceutically acceptable salt is derived from hydrochloric acid.

7. (Original) The composition of claim 1, wherein the composition inhibits, regulates and/or modulates tyrosine kinase signal transduction.

8. (Original) The composition of claim 7, wherein the tyrosine kinase is a receptor-type and/or non-receptor type tyrosine kinase.

9. (Original) The composition of claim 1, wherein the cancer is selected from the group of cancers consisting of cancers of the breast, leukemia, melanoma, stomach, colon, central nervous system (CNS), ovarian and prostate and lung.

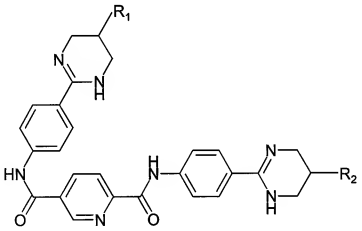
10. (Original) The composition of claim 1, wherein the cancer is selected from the group consisting of chronic myelogenous leukemia (CML), acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL).

11. (Original) The composition of claim 4, wherein the cancer is selected from the group consisting of chronic myelogenous leukemia (CML) and acute lymphoblastic leukemia (ALL).

12. (Original) The composition of claim 1, wherein the composition is administered orally or parenterally.

13. (Original) The composition of claim 1, wherein the composition further comprises an anti-cancer agent.

14. (Original) A method for treatment of cancer involving inappropriate tyrosine kinase activity in a mammal in need of such treatment, said method comprising administering to said mammal a therapeutically effective amount of a compound selected from the group consisting of Formula I, a pharmaceutically acceptable salt thereof, a stereoisomer thereof, and mixtures thereof:

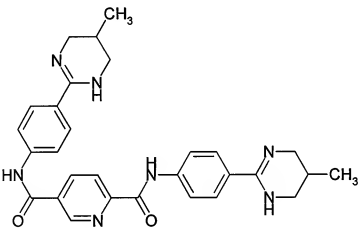


Formula I

wherein R_1 and R_2 are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; halogen; aryl; heteroaryl containing N, O, or S; the aryl and heteroaryl may be further substituted with halogen, an alkyl, alkenyl, and alkynyl; NZ_1Z_2, wherein Z_1 and Z_2 are independently selected from the group consisting of H and alkyl; and (CO)Y wherein Y is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl containing N, O, or S; with the proviso that when R_1 is hydrogen, R_2 is a group other than hydrogen.

15. (Original) The method of claim 14, with the proviso that when R_1 is methyl, R_2 is a group other than methyl.

16. (Original) The method of claim 14, wherein the compound is selected from the group consisting of Formula II, a pharmaceutically acceptable salt thereof, a stereoisomer thereof, and mixtures thereof:



Formula II

17. (Original) The method of claim 14 in combination with a therapy selected from the group consisting of radiation therapy and chemotherapy.

18. (Original) The method of claim 14, wherein the cancer is selected from the group of cancers consisting of cancers of the breast, leukemia, melanoma, stomach, colon, central nervous system (CNS), ovarian and prostate and lung.

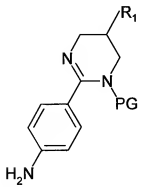
19. (Original) The method of claim 18, wherein the cancer is selected from the group consisting of chronic myelogenous leukemia (CML), acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL).

20. (Original) The method of claim 16, wherein the cancer is selected from the group consisting of chronic myelogenous leukemia (CML) and acute lymphoblastic leukemia (ALL).

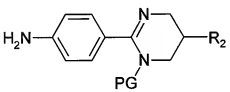
21. (Original) The method of claim 14, wherein the therapeutically effective amount is between about 0.1 mg/kg of body weight up to less than about 50 mg/kg of body weight per day.

22. (Original) The method of claim 21, wherein the therapeutically effective amount is between about 0.5 mg/kg of body weight to about 25 mg/kg of body weight per day.

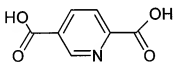
23. (Original) A method for making the compound of claim 1 comprising reacting:



and



wherein PG is a protecting group, with

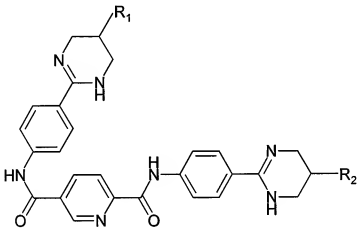


in the presence of a coupling catalyst for promoting amide bond formation, and removing the protecting groups.

24. (Original) The method of claim 23, wherein the coupling catalyst is a mixture of HBTU (O-Benzotriazol-1-yl-N,N,N',N'-tetramethyluronium hexafluorophosphate) or HATU (O-(7-Azabenzotriazole-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate); DIPEA (N,N-diisopropylethylamine); and HOBt (1-hydroxybenzotriazole).

25. (Original) The method of claim 23, wherein the deprotection step comprises the addition of a saturated solution of hydrochloric acid in methanol.

26. (NEW) A compound selected from the group consisting of Formula I, a pharmaceutically acceptable salt thereof, a stereoisomer thereof, and mixtures thereof:

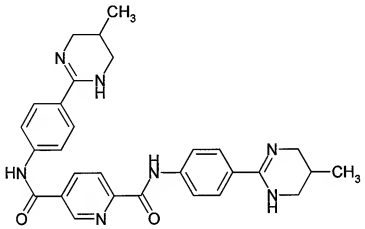


Formula I

wherein R_1 and R_2 are independently selected from the group consisting of H; alkyl; alkenyl; alkynyl; halogen; aryl; heteroaryl containing N, O, or S; the aryl and heteroaryl may be further substituted with halogen, an alkyl, alkenyl, and alkynyl; NZ_1Z_2, wherein Z_1 and Z_2 are independently selected from the group consisting of H and alkyl; and (CO)Y wherein Y is selected from the group consisting of H, alkyl, alkenyl, alkynyl, aryl, heteroaryl containing N, O, or S; with the proviso that when R_1 is hydrogen, R_2 is a group other than hydrogen; and when R_1 is methyl, R_2 is a group other than methyl.

27. (NEW) The compound of claim 26, wherein the aryl and heteroaryl are substituted with at least one of a halogen, an alkyl, an alkenyl, and an alkynyl.

28. (NEW) The compound of claim 26, wherein the compound is selected from the group consisting of Formula II, a pharmaceutically acceptable salt thereof, a stereoisomer thereof and mixtures thereof:



Formula II

REMARKS

Upon entry of this Preliminary Amendment, claim 3 has been amended, and claims 26, 27, and 28 are newly added. Support for claims 26-28 are described at page 3, line 13 to page 5 line 13, and at page 10, line 31 to page 11, line 10 of the detailed description. It is believed that the foregoing amendments and additions add no new matter to the present application.

Favorable action in regard to the application is earnestly solicited.

Respectfully submitted ,

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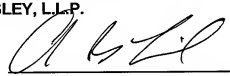
By: 

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